CALIFORNIA ENVIRONMENTAL PROTECTION AGENCY
DEPARTMENT OF PESTICIDE REGULATION
MEDICAL TOXICOLOGY BRANCH

SUMMARY OF TOXICOLOGY DATA
5-CHLORO-2-(2,4,-DICHLORO- PHENOXY) PHENOL

Chemical Code # 001371, Tolerance # 50291
SB 950 # 568

Original Date: September 10, 2003

DATA GAP STATUS

Combined (Chronic/onco), rat: **Data gap, inadequate study, adverse effects not determined**

Combined (Chronic/onco), hamster: **No data gap, no adverse effect**

Chronic toxicity, dog: **Data gap, no study submitted**

Reproduction, rat: **Data gap, no study submitted**

Teratology, rat: **No study submitted**

Teratology, rabbit: **Data gap, inadequate study, possible adverse effect indicated.**

Teratology, mouse: **Data gap, inadequate study, possible adverse effect indicated**

Gene mutation: **Data gap, inadequate studies, adverse effects indeterminate**

Chromosomal aberrations: **Data gap, inadequate studies, no adverse effect indicated.**

DNA damage: **Data gap, inadequate studies, no adverse effect indicated.**

Neurotoxicity: **Not required at this time**

Toxicology one-liners are attached.

All record numbers through 175832 were examined.
**** indicates an acceptable study.**
Bold face indicates a possible adverse effect.

File name: T030910
Original by: Kishiyama & Silva, 9/10/03

This chemical is registered as an antimicrobial for use in fabrics. It is also used in skin products.

II. TOXICOLOGY ONE-LINERS AND CONCLUSIONS

These pages contain summaries only. Individual worksheets may contain additional effects.

COMBINED, RAT

50291 - 007, 008, & 009 045802 "FAT 80'023 2-Year Oral Administration to Rats," (Yau, E.T., Green, J.D.; CIBA-GEIGY Corporation, Research Department, Chemicals Division, Greensboro, NC; Report #: 85152; 4/28/86). FAT 80'023 (purity = 99%) was fed in diet to Sprague-Dawley rats [Crl: COBS® CD® (SD) BR] (60/sex/dose) at 0, 300, 1000 and 3000 ppm for 104 weeks. At 0, 300, 1000 and 3000 ppm, an additional 5/sex/dose were added for sacrifice at weeks 13, 26, and 78. At 52 weeks, 20/sex/dose were added for sacrifice at 0 and 6000 ppm and 10/sex/dose for all other doses. At week 78 for the chronic study, 60/sex/dose were sacrificed at 0, 300, 1000 and 3000 ppm. Chronic NOEL = Not determined due to an illegible pathology report. Male body weights were statistically significantly lower than control weeks 2 - 52 at 6000 ppm and through week 8 at 3000 ppm. Female body weights were statistically significantly lower at ≥ 3000 ppm. There was a statistically significant increase in food consumption at ≥ 3000 ppm in males. Absolute and relative male liver weights were decreased at ≥ 3000 ppm. There was a decrease in absolute heart and a decrease in relative kidney and brain weights in males at 6000 ppm. Absolute brain weights in males were decreased at 3000 ppm. Females showed decreased absolute heart and liver weights and increased relative brain, kidneys, ovaries, heart and adrenals at 6000 ppm and increased absolute and relative ovary weights and decreased relative spleen weights at 3000 ppm. There were numerous hematology, and clinical chemistry parameters affected in both sexes throughout the study, primarily at ≥ 1000 ppm. Urinary protein was not statistically significantly decreased, but was lower at ≥ 3000 ppm in females. No evidence of treatment-related oncogenicity. Not acceptable ("Pathology Report for Individual Animal" Appendix VI-7 was illegible, therefore it is not possible to determine the presence of a possible adverse effect) but possibly upgradeable upon submission of a legible copy of the "Pathology Report for Individual Animal" and the full report for the 90-day study supporting dose selection.) (Silva, 4/9/03).

50291 - 023 119775, addendum to: 007, 008, 009 045802 Subchronic Study (in DPR volume/record #: 50291 - 023/119775): "Pathology Working Group Report on Triclosan 90-Day Subchronic Toxicity Study in Sprague-Dawley Rats," was presented in brief summary, submitted in conjunction with the Pathology Work Group (PWG, D.G. Goodman, J.M. Cullen, P.M. Newberne, R.A. Squire, J.M. Ward, R.M. Sauer) review for the definitive 2-Year Chronic Rat Study (DPR volume/record #: 50291 - 007 - 009/045802). Some of the pathology from the 90-day subchronic study was reviewed by Pathco, Inc., Ijamsville, MD, which headed the PWG. Results of the evaluation of the liver pathology for the subchronic study, the PWG deemed 3000 ppm to be an appropriate MTD for the definitive study. Two Year Chronic Study: Liver and lung histopathology from "FAT 80'023 2-Year Oral Administration to Rats," (Yau, E.T., Green, J.D.; CIBA-GEIGY Corporation, Research Department, Chemicals Division, Report 85152; 4/28/86) was evaluated by the PWG and their findings were submitted in DPR volume/record #: 023/119775 ("Irgasan® DP 300 Pathology Working Group (PWG) Report on Triclosan/Carcinogenicity Study in Sprague-Dawley Rats; Additional Data to Support Acceptance of MRID 161332," Goodman, D.G.; Pathco, Inc., Ijamsville, MD; 1/23/90). Since data from the definitive study were in question and were re-evaluated by a "PWG", it must be clarified that the term "PWG"does not equate to that term as used by US EPA. "PWG" as defined by US EPA, consists of 3 independent pathologists, who evaluate the data in question, without consulting one

another or the original Study Pathologist. Therefore, although some data were re-reviewed by a Pathco, Inc. - devised work group, the information (for the purpose of upgrading the study) is considered supplemental, and the original data (until re-examined by a US EPA PWG) will be the primary data considered by DPR reviewers. As of September 2, 2003, a readable copy of the animal pathology for the definitive study has not been received at DPR. All pathology must be evaluated by DPR prior to determining the acceptability of the 2-Year Chronic Rat Study. The definitive study remains unacceptable but upgradeable with submission of a readable histopathology report. (Kishiyama & Silva, 9/2/03).

COMBINED, HAMSTER

** 50291 - 028 175832 "Potential Tumorigenic and Chronic Toxicity Effects in Prolonged Dietary Administration to Hamsters," (Chambers, P.R.; Huntingdon Life Sciences Ltd., Huntingdon, England; CBG 756/972896; 3/30/99). FAT 80'023/S (purity = 99.5%) was fed in diet to Bio FID Alexander Syrian hamsters (Main group = 60/sex/dose; satellite = 10/sex/dose) at 0 (2 control groups), 12.5, 75, or 250 mg/kg for 90/95 weeks (Main Group; 90 weeks &;95 weeks %) and 52 weeks (Satellite). Chronic NOEL = 75 mg/kg (Mortality was statistically significantly increased at 250 mg/kg. General clinical condition deteriorated at 250 mg/kg (lethargy, hunched posture, pallor, thin appearance, unsteady gait). Body weight change was lower throughout the dosing period in both sexes at 250 mg/kg. Food consumption during weeks 1 - 3 was decreased in both sexes at 250 mg/kg. However all food consumption decreases were minimal even though they were statistically significant. Water consumption was increased at 250 mg/kg. Urine volume was increased and specific gravity was decreased in both sexes throughout the study at 250 mg/kg. Protein levels and pH values of urine were decreased in both sexes during the first 52 weeks of study at 250 mg/kg. There was an increased incidence in macroscopic irregular cortical scarring and pale coloration of kidneys in both sexes at 250 mg/kg. Females also had a macroscopic increase in white nodules of forestomach at 250 mg/kg. There was a statistically significant increase in distended medullary tubules in males and in radial areas of dilated basophilic kidney tubules in both sexes at 250 mg/kg. The incidence of nephropathy was statistically significantly increased in both sexes at 250 mg/kg. There was a statistically significantly increased incidence in partial depletion of one or more generations of germ cells in testes and in absent spermatozoa, in abnormal spermatogenic cells and in reduced numbers of spermatozoa in epididymides in males at 250 mg/kg. Focal atypical hyperplasia in the fundic region of the stomach was statistically significantly increased in males at 250 mg/kg. The incidence of distended gastric gland (sometimes containing debris) was statistically significantly increased in both deceased and terminal females at 250 mg/kg. Platelets, GPT and urea nitrogen were decreased at 250 mg/kg in both sexes. PCV, RBC and Hb were decreased in females at 250 mg/kg. WBC and triglycerides were increased in both sexes at 250 mg/kg.) There was no treatment-related oncogenicity. Acceptable, with no adverse effect. (Kishiyama & Silva, 9/4/03).

CHRONIC, BABOON

50291 - 010 045805 "A 1 Year Oral Toxicity Study in Baboons with Compound FAT 80 023/A," (Drake, J.C.; CIBA-GEIGY Pharmaceuticals Wilmslow, Cheshire, UK; Report #: 169/75/S.L; 7/28/75). FAT 80 023/A (purity not stated) administered orally in gelatin capsules to Papio Baboons (7/sex/dose) at 0 (600 mg lactose + 0.5% magnesium stearate), 30, 100 and 300 mg/kg. After 6, 12 and 13 months (including 28-day recovery period), 2, 3 and 2 baboons/sex/dose, respectively, were sacrificed. NOEL = 30 mg/kg (Body weight gain was slightly decreased in males at $\geq$ 100 mg/kg and in females at 300 mg/kg by study termination (week 52). Diarrhea and vomiting were observed in both sexes at $\geq$ 100 mg/kg. Food intake was decreased in males at 300 mg/kg, however statistical significance was not achieved at any particular time point. At 300 mg/kg, females showed an increased incidence in loss of condition (3/6) self-inflicted injury to

anal pads (1/6), abrasion (1/6), abdominal pain (2/6), ulcers on feet and anal pads (1/6), no feces passed (1/6) and lethargy (1/6). In females there was a statistically significant increase in prothrombin time and a decrease in Hb, RBC and PCV% at 300 mg/kg. There were no treatment-related long term effects to body weight gain, food consumption, clinical signs, necropsy or histopathology after the recovery period.) UNACCEPTABLE (too few animals at scheduled termination and insufficient information) not upgradeable. (Kishiyama & Silva, 4/23/03)

CHRONIC TOXICITY, DOG

No study submitted

ONCOGENICITY, RAT

See combined (Chronic/Oncogenicity), rat

ONCOGENICITY, MOUSE

No study submitted

REPRODUCTION, RAT

50291 - 011 045806 "Two-Generation Reproduction Study in Rats," (Morseth, S.L., Hazleton Laboratories America, Inc., Vienna, VA; Project #: 2386-100 amendment #1; 12/11/85). This volume contains an amendment to a reproduction study protocol. No worksheet. M. Silva, 9/10/03.

TERATOLOGY, RAT

No study submitted

TERATOLOGY, MOUSE

50291 - 011 045808 "Irgasan DP 300: Effect of GP 41'353 on Pregnancy of the Mouse," (A.K. Palmer, G.M. Scarles; Huntingdon Research Centre, Huntingdon, England, Report #: 2374/68/251; 8/26/68) GP 41'353 (Batch #: Mg2, purity not stated) was administered via oral gavage to mated CD-1 mice (16 - 21) at 0, 10, 50 and 100 mg/kg during gestation days 1 through 16. Maternal NOEL = 10 mg/kg (There was an increased incidence in maternal death at $\geq$ 50 mg/kg (1 at 50 mg/kg & 6 at 100 mg/kg). Clinical observations (found only in the animals that died) were pilo-erection, weight loss and respiratory distress and were reported to be related to tympanites (enteric disorder causing gas/air in intestine or peritoneal cavity). There were no

statistically significant treatment-related effects on body weight and body weight gain, however they were depressed at 100 mg/kg.). Developmental NOEL = 10 mg/kg (There was an increased incidence in percentage of skeletal effects (sternebrae bipartite and/or asymmetrical) in fetuses at 100 mg/kg. There was an increased incidence in percentage of extra ribs in fetuses at ≥ 50 mg/kg. Total percentage of fetuses with variants was statistically significantly increased in all treated groups. However there was no analysis of data on a per litter basis and there were no historical controls for the above effects to fetuses or litters.) Possible adverse effect indicated (Increased fetal variations and maternal death at ≥ 50 mg/kg). Not acceptable and not upgradeable (numerous deficiencies). The data are supplemental. (Kishiyama & Silva, 6/11/03).

TERATOLOGY, RABBIT

50291 - 011 045809 "Irgasan DP 300: Effect of GP 41'353 on pregnancy of the New Zealand White Rabbit," (Palmer, A.K., Readshaw, M.A; Huntingdon Research Centre, Huntingdon, England, Report #: 2403/68/280; 9/26/68). GP 41'353 (Batch #: Mg2, purity not stated) was administered via oral gavage to mated New Zealand White rabbits (13/dose) at 0, 10, 25, or 50 mg/kg during gestation days 6 through 18. Maternal NOEL = 10 mg/kg (There was an increase in total litter resorption at ≥ 25 mg/kg and a decrease in number of litters at C-section at 50 mg/kg.) Developmental NOEL = 25 mg/kg (There was an increase in 13 ribs on a per fetus level at 50 mg/kg, however, there were no "per litter" calculations. In addition, the increase (although statistically significant) was within historical control range.) Possible adverse effect indicated: There was an increased incidence in total litter resorptions at ≥ 25 mg/kg. Not acceptable and not upgradeable. (Kishiyama & Silva, 6/24/03)

GENE MUTATION

50291 - 011 045812 *"Salmonella*/Mammalian-Microsome Mutagenicity Test with FAT 80 023/A," (Arni P., Müller. D.; CIBA-GEIGY Limited; Basle, Switzerland, Experiment #: 78-2511; 3/1/78). FAT 80 023/A (purity unstated) was tested on *Salmonella typhimurium* strains TA98, TA100, TA1535, TA1537 at 0, 0.01, 0.03, 0.09, 0.27, 0.81, 2.43 and 7.29 μg/0.1 ml (+ S9 metabolic activation) and at 0.01, 0.03, 0.09, 0.27 and 0.81 μg/0.1 ml (no S9) to evaluate mutagenic potential. In addition 2.43 and 7.29 μg/0.1 ml were tested (no S9) on TA92 (3 plates/test condition).. FAT 80 023/A treatments (+/- S9) did not increase the number of histidine-phototropic mutants. At ≥ 0.09 μg/0.1 ml (no S9) and at 7.29 μg/0.1 ml (+S9) bacterial growth was inhibited. All positive controls showed a significant increase in the incidence of histidine-phototropic mutants. The study is not acceptable and not upgradeable due to numerous deficiencies. No adverse effect indicated. (Kishiyama & Silva, 6/30/03).

50291 - 011 045813 "Mutagenic Effects of "Irgasan" on *Drosophila melanogaster*," (Magnusson, J.; Wallenberg Laboratory, University of Stockholm, Sweden, 1/30/79). Irgason (purity not stated) was dissolved in corn oil or sucrose was mixed in corn agar substrate and fed to *Drosophila melanogaster* (3 broods of male fruit flies) at 100 ppm (sucrose) and 1000 ppm (sucrose & corn oil) to test for sex-linked recessive lethals. Three experiments were performed: 1) Mutagenicity Test: Feeding was performed in ordinary vials containing corn agar substrate and males received 1000 ppm (Irgasan dissolved in corn oil) for 7 days. 2) Feeding (24 hours) was performed in glass tubes (13 ml) with a piece of Kleenex tissue in the bottom to which ½ ml of the sucrose solution at 100 and 1000 ppm were added. 3) The Irgasan Uptake Analysis: Performed on animals injected with Ringer solution at 1000 ppm or fed with corn oil. Uptake was measured at 0, 24, 48 and 72 hours

(feeding) or at 0, 24 and 48 hours (injection). Experiments were performed using three broods of males. No increase in sex-related recessive lethals was reported. This study is not acceptable and not upgradeable (deficiencies too numerous). Without a positive control, conclusions cannot be made. **(Kishiyama & Silva, 6/30/03).**

50291 - 011 045815 "Point Mutation Assay with Mouse Lymphoma Cells I. *In Vitro-Test* / II. Host mediated Assay with FAT 80 023/A," (Strasser, F.F., Müller, D.; CIBA-GEIGY Limited; Basle, Switzerland, Experiment: 78-2305 & 78-2306; 5/10/78). FAT 80 023/A (purity not stated) was assayed with L5178Y mouse lymphoma cells (2 flasks/dose/incubation time, 10^6 cells/ml in semisolid agar) at 0 (2% carboxymethyl cellulose),15.8 µg/ml (18 hour incubation) and 28.9 µg/ml (4 hour incubation), followed by a 3 day, treatment-free incubation to assess incidence of mutants. In a host-mediated assay, 10^6 L5178Y cells were injected intraperitoneally into DBA/2f/Bom (SPF) mice (4/dose, sex not stated). Three days after inoculation, mice were dosed orally at 0 (2%, CMC, 10ml/kg) and 1313 mg/kg. Three days later the cells were removed from the peritoneal fluid and seeded into flasks and the incidence of mutation was determined. Results showed no treatment-related increase in the number of mutant L5178Y colonies after either *in vivo* or *in vitro* exposure. No adverse effect indicated. Not acceptable or upgradeable, due to numerous deficiencies. Kishiyama & Silva, 8/1/03

50291 - 011 045819 "The Effect of Irgasan DP 300 in the "Mammalian Spot Test", an *In Vivo* Method for the Detection of Genetic Alterations in Somatic Cells of Mice," (Fahrig, R.; Zentrallaboratorium für Mutagenitätsprüfung der Deutschen Forschungsgemeinschaft; 6/22/78). Irgasan DP 300 (99.7% pure) was injected into the peritoneal cavity **of mated C57BL/6JHan female mice on gestation day 10 at 0 (Hank's balanced salt solution) and 50 mg/kg to 46 or 43 females, respectively. Embryos of the genotype a/a; b/+; c^{ch}p/++; d se/++ and s/+ (heterozygous for 4 different recessive coat-color genes) received treatment *in utero* during the 10^{th} day of gestation when about 200 pigment precursor cells were available. The author of the report stated: "The frequency of color spots in mice in the test and control groups clearly show that Irgasan DP 300 in a dose of 50 mg/kg is active in the spot test. So it is hardly necessary to use any statistics." The control frequency of color spots was 0.1%, compared with 2.4% with Irgasan DP 300**. The mutagenicity of Irgasan DP 300 was considered in the report to be of medium potency. Possible adverse effect indicated: There was an increased incidence in color spots in treated animals. This study is not acceptable and not upgradeable due to numerous deficiencies and primarily the lack of a positive control. (Kishiyama & Silva, 8/25/03)

50291 - 011 045814 "Intrasanguine Host-Mediated Assay with *S. typhimurium* With FAT 80 023/A," (Arni, P., Müller, D.; CIBA-Geigy Limited, Basle, Switzerland; Experiment #: 78/2803; 3/27/79). FAT 80 023/A (purity not stated) was administered by gavage at 0 (2% carboxymethyl cellulose), 50, 100, 200 and 400 mg/kg in 3 doses at 2, 1 and 0 hours immediately prior to tail vein injection in male mice (6/dose) of *Salmonella typhimurium* strains TA98, TA100, TA1535 and TA 1537. After 60 minutes, mice were sacrificed and the livers processed. Aliquots were plated for bacterial counts (nutrient broth plates) and mutants (minimal agar plates). There was no treatment-related effect on bacterial count, nor was there an increase in mutation rate. There were, however, no positive controls. Unacceptable (Insufficient information, deficiencies too numerous). Not upgradeable. (Kishiyama & Silva, 7/1/03)

50291 - 011 045820 "Use of the Mouse Spot Test to Investigate the Mutagenic Potential of Triclosan (Irgasan7 DP 300)," (Russell, L.B., Montgomery, C.S.; Published in: Mutation Research, 79:7-12, 1980). Triclosan (99.7% pure) was administered in a single I.P. dose to impregnated inbred C57BL/E females (3 - 6 months of age) at 0 (60% methanol), 1 - 4, 8 or 25 mg/kg on days 9.25 or 10.25 postconception to assess effects in an *in vivo* somatic mutation test (spot test). Dose ranges overlapped

the toxic (8 mg/kg reduced post natal survival and 25 mg/kg was toxic to mothers and fetuses exposed *in utero*). Incidence of recessive spots was not significantly increased with triclosan under the conditions of this study. A comparison was made with the study reported by Fahrig et al. (DPR volume/record #: 50291 - 011 045819), where Irgasan DP 300 was used. The authors claim triclosan is insoluble in HBSS (used as a solvent in the Fahrig study) and that dosages at 50 mg/kg were sufficiently toxic in the current study as to make it impossible to obtain enough survivors for evaluation. These authors claim that in the Fahrig study, little or no Irgasan DP 300 was in solution in the study and the 2.4% incidence in color spots was questioned. Not acceptable and not upgradeable due to the fact that this was an open literature study and not performed according to FIFRA Guidelines. No adverse effect indicated. (no work sheets). (Kishiyama & Silva, 8/25/03).
CONCLUSION: There were adverse effects indicated in one study (50291 - 011 045819), however this study was not acceptable or upgradeable (no positive control). None of the other studies were acceptable or upgradeable either, therefore, it is not possible at this time to determine whether FAT 80'023/S induces gene mutations.

CHROMOSOME EFFECTS

50291 - 011 045816 "Dominant Lethal Study," (Fritz, H.; CIBA-GEIGY Limited, Basle, Switzerland, experiment 32710200; 10/20/71). GP 41 353, was administered in a single gavage treatment to albino male mice (12/dose) at 0 (2% carboxymethylcellulose), 750, or 1500 mg/kg. Subsequently, the males were mated weekly, for 8 weeks, to untreated females (3 females/male/mating; fresh group of females/mating). Results showed no evidence of treatment-related dominant lethal effects. There were no treatment-related decreases in the number of implantations or increases in embryonic deaths (resorptions). Although there were no statistically significant differences in mating ratio, the number of successful matings overall was reduced approximately 10% for GP 41 353 treated animals. Historical controls were not included. No evidence of dominant lethal on the progeny of males treated with GP 41 353. Not acceptable and not upgradeable due to numerous deficiencies. No adverse effect indicated. (Kishiyama & Silva, 8/4/03).

50291 - 011 045821 "Chromosome Studies on Somatic Cells - GP 41 353 (Triclosan)," (Müller, D., Strasser, F.F.; Pharmaceuticals Division, Toxicology/Pathology; CIBA-GEIGY Limited, Basle, Switzerland; 4/16/73). GP 41 353 was administered to Chinese hamsters (4/dose) by gavage for 2 consecutive days at 0 (0.5% CMC),150, 300 and 600 mg/kg to test for mutagenic effects on bone marrow cells. Animals were sacrificed 4 hours after the last dose, femoral bone marrow was removed and prepared for chromosomal analyses. There were no treatment-related increases in chromosomal aberrations at any dose. The positive controls performed as expected. No adverse effect indicated. The study is not acceptable and not upgradeable, due to numerous deficiencies. (Kishiyama & Silva, 8/26/03).

50291 - 011 045822 "Chromosome Studies in Somatic Cells -- Long Term Study With FAT 80 023/A Chinese Hamster (Test for mutagenic effects on bone marrow cells)," (Strasser, F.F., Müller, D.; CIBA-GEIGY Limited, Basle, Switzerland, Experiment #78-3105; 2/15/79). FAT 80 023/A (purity not stated) was administered by gavage to Chinese hamsters (6/sex/dose) 3 times weekly for 12 weeks at 0 (0.7% Carboxymethyl cellulose), 75, 150, 300 and 600 mg/kg to assess the effects on bone marrow cell chromosomes. There were no treatment-related effects observed at any dose. It was not possible to form conclusions in this study due to a lack of positive and historical controls. Not acceptable and not upgradeable due to numerous deficiencies. No adverse effect indicated. (Kishiyama & Silva, 8/27/03).

50291 - 011 045823 "Nucleus Anomaly Test on Somatic Interphase Nuclei - GP 41 353 (Triclosan)," (Langauer, M., Müller, D.;.CIBA-GEIGY Limited, Basle, Switzerland; 5/31/74). GP 41 353 (purity not stated) was administered by gavage to Chinese hamsters (3/sex/dose) for 2 consecutive days at 0 (0.5% CMC), 150, 300 and 600 mg/kg to assess effects on somatic interphase cells *in vivo*. There was no treatment-related increase in micronuclei. The positive control (cyclophosphamide) functioned as expected. This study is not acceptable and not upgradeable due to numerous deficiencies. No adverse effect indicated. (Kishiyama & Silva, 8/27/03).

50291 - 011 045824 "Nucleus Anomaly Test in Somatic Interphase Nuclei Long-Term Study with FAT 80 023/A; Chinese Hamster (Test for mutagenic effects on bone marrow cells)," (Langauer, M., Müller, D.; CIBA-GEIGY Limited, Basle, Switzerland, Experiment #73-3005; 8/23/78). FAT 80 023/A (purity not stated) was administered by gavage to Chinese hamsters (6/sex/dose) 3 times weekly for 12 weeks at 0 (0.7% CMC), 75, 150, 300 and 600 mg/kg to assess the effects on bone marrow cells. One thousand cells from 3/sex/group were evaluated for micronuclei and polyploidy. There were 7/12 deaths at 600 mg/kg. There were no treatment-related effects observed at any dose. Not acceptable and not upgradeable due to numerous deficiencies. Since there were no positive or historical controls or clinical signs described, it is not possible to make conclusions about the toxicity of FAT 80 023/A under the test conditions. No adverse effect indicated. (Kishiyama & Silva, 8/27/03).

50291 - 011 045817 "Chromosome Studies in Male Germinal Epithelium," (Hool, G., Strasser, F.F., Müller, D.; CIBA-GEIGY Limited, Basle, Switzerland; Experiment #: 78-2903; 12/1/78). FAT 80 023/A (purity not stated) was administered via gavage to NMRI male mice (8/dose) at 0, 189, 378, 756 and 1512 mg/kg/day for 5 consecutive days. The testes were processed (no details) and drop preparations made. 100 metaphases from each of 6 animals per dose were scored. Results showed a single chromosome aberration in the form of a minute (acentric chromosomal fragment) at 756 mg/kg. Seven animals died at 1512 mg/kg. Subsequently a dose group at 189 mg/kg was added. No adverse effect indicated. This study is not acceptable or upgradeable due to numerous deficiencies. (Kishiyama & Silva, 8/22/03)

50291 - 011 045818 "Chromosome Studies in Male Germinal Epithelium," (Hool, G., Strasser, F.F. Müller, D.; CIBA-GEIGY Limited, Basle, Switzerland, Experiment #: 78-2904; 2/21/79). FAT 80 023/A (Batch #: 652, purity not stated) was administered via gavage to NMRI-derived male mice (8/dose) on days 0, 2, 3, 5 and 9 at 0, 189, 378, 756 and 1512 mg/kg. Three days after the last dose, mice were sacrificed and drop preparations were made of the testicular parenchyma. 100 metaphases of spermatocytes for 6 per group were scored. There were no treatment-related increases in chromosomal aberrations at any dose. The study is not acceptable or upgradeable, due to numerous deficiencies. No adverse effect indicated. (Kishiyama & Silva, 8/22/03).

DNA DAMAGE

50291 - 011 045811 "Mutagenicity Test on *Saccharomyces cerevisiae* MP-1 *In Vitro with* FAT 80 023/A," (Arni P., Müller, D.; CIBA-GEIGY Limited, Basle, Switzerland; Experiment #: 78/3402; 11/27/78). FAT 80 023/A (purity not stated) was tested on *Saccharomyces cerevisiae* strain MP-1 at 10, 20, 30, 40, 50, 60, and 200 mg/l to evaluate genotoxic potential. Incubation was for 3 ½ hours without activation only (20 plates/condition). There were no treatment-related effects at any concentration. The positive control functioned as expected. This study is not acceptable and not upgradeable (numerous deficiencies). No adverse effect indicated. (Kishiyama & Silva, 6/27/03)

50291 - 011 045810 "Genetic Activity of Irgasan DP 300 in the MP-1 Strain of S. cerevisae," (Fahrig, R.; Zentrallaboratorium für Mutagenitätsprüfung der Deutschen Forschungemeinschaft; 6/22/78) Irgasan DP 300 (99.7% pure) was tested with *S. cerevisae* MP-1 strain at 0 and 0.2 mg/ml to evaluate it's genotoxic potential. Treatments were tested on complete media for survival and intergenic recombination and on selective media with actidione for mutation and without tryptophan for interallelic recombination data without activation only. Three tests with 20 replicates per condition. This study is not acceptable and not upgradeable. The report stated that "Irgasan DP 300 shows weak, but definite mutagenic and recombinogenic activity in *S. cerevisiae* strain MP-1," (page 9). The deficiencies were too numerous and too critical to make this study upgradeable. (Kishiyama & Silva, 6/25/03).